

AMENDMENTS TO THE CLAIMS

This listing of the claims replaces all prior listings and versions:

1. (currently amended): A method of selecting a switching system, the switching system comprising: (i) a first component comprising a first ~~molecule~~ polypeptide and (ii) a second component comprising a second ~~molecule~~ polypeptide, in which the first ~~molecule~~ polypeptide binds to the second ~~molecule~~ polypeptide in a manner modulatable by a ligand, and (iii) a third component comprising the ligand, and wherein at least one of the first or second polypeptides binds to DNA, the method comprising the steps of:

- (a) contacting one or more candidate first ~~molecules~~ polypeptides with one or more candidate second ~~molecules~~ polypeptides in the presence of one or more ligands,
- (b) selecting a complex of the three components;
- (c) optionally isolating and/or identifying the unknown components of the complex;
- (d) comparing the binding of the first ~~molecule~~ polypeptide component of the complex to the second ~~molecule~~ polypeptide component of the complex in the presence and absence of the ligand component of the complex; and
- (e) selecting complexes where said binding differs in the presence and absence of the ligand component,

in which at least one component is provided in the form of a library of members.

2. (currently amended): A method according to Claim 1, in which at least one of the candidate first ~~molecules~~ polypeptides comprises a non-naturally occurring binding domain which binds to the second ~~molecule~~ polypeptide.

3. (currently amended): A method according to claim 1, in which ~~one of the first molecule and second molecule~~ polypeptides binds to DNA ~~comprises a nucleic acid binding molecule, and the other of the first and second molecules comprises a nucleic acid.~~

4. (currently amended). : A method according to Claim 1, in which one or both of the first and second polypeptides ~~candidate nucleic acid and nucleic acid binding molecules~~ is provided as a plurality of molecules.

5. (currently amended): A method according to Claim 4, in which the plurality of molecules is nucleic acid binding molecule is provided as a library of nucleic acid binding molecules.

6. (canceled).

7. (withdrawn): A method according to Claim 4, in which one of the components isolated and/or identified in step (c) is a ligand component.

8. (currently amended): A method according to claim 4, in which one of the components isolated in step (c) is a polypeptide that binds to DNA ~~nucleic acid binding molecule component~~.

9. (canceled).

10. (withdrawn): A method according to claim 4, in which a plurality of candidate ligands are used.

11. (withdrawn): A method according to claim 4, in which the ligands are provided as a library of ligands.

12. (canceled).

13. (currently amended): A method according to claim 1 ~~claim 4~~, in which ~~the one or both of the first or second polypeptides are at least partly derived from DNA binding proteins, preferably~~ transcription factors.

14. (currently amended): A method according to claim 13 ~~claim 4~~, in which the ~~candidate nucleic acid binding molecules are derived from~~ transcription factor is a zinc finger transcription factors.

15. (currently amended): A method according to claim 1 ~~claim 4~~, in which one or both of the first or second polypeptides ~~the candidate nucleic acid binding molecules~~ are provided as a phage display library.

16. (withdrawn): A method according to claim 4, in which the ligand is selected from Distamycin A, Actinomycin D and echinomycin.

17. (withdrawn): A switching system comprising a gene switch, in which the switching system has been selected by a method according to claim 4.

18. (currently amended): A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a ~~nucleic acid binding molecule~~ switching system selected according to the method of claim 1 ~~claim 4~~ binds in a manner modulatable by a ligand and binding the ~~nucleic acid binding molecule~~ switching system to the target nucleic acid such that transcription is regulated.

19 and 20. (canceled).

21. (currently amended): A method of modulating the expression of one or more genes, said method comprising administering a ~~nucleic acid binding molecule~~ switching system and a ligand selected according to the method of claim 1 ~~claim 4~~ to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid ~~selected according to the method of claim 4~~.

22. (currently amended): A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a nucleic acid sequence capable of directing the expression of a ~~nucleic acid binding molecule~~ switching system selected according to the method of claim 1 and a target nucleic acid sequence to which the ~~nucleic acid binding molecule~~ switching system binds in a manner modulatable by a ligand, which method comprises administering said ligand to the cell and wherein the ~~nucleic acid binding molecule~~ switching system is heterologous to the host cell.

23. (withdrawn): A method according to Claim 21 wherein the host cell is a plant cell.

24. (withdrawn): A method according to Claim 23, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

25. (withdrawn): A non human transgenic organism comprising a target nucleic acid sequence and a nucleic acid sequence capable of directing the expression of a nucleic acid binding molecule which binds to the target nucleic acid in a manner modulatable by a ligand, in which the target nucleic acid sequence and/or nucleic acid sequence are heterologous to the organism.

26. (withdrawn): A transgenic non-human organism according to Claim 25 which is a plant.

27 to 30. (canceled).

31. (currently amended): A method according to claim 1 ~~27~~, in which the ligand is an immunoglobulin molecule, preferably an antibody molecule.

32 to 33. (canceled)

34. (currently amended): A switching system comprising a protein switch comprising: (i) a first component comprising a first polypeptide and (ii) a second component comprising a second polypeptide, in which the first polypeptide binds to the second polypeptide in a manner modulatable by a ligand, and (iii) a third component comprising the ligand, wherein at least one of the first or second polypeptides binds to DNA, and in which the switching system has been selected by a method comprising the steps of:

- (a) contacting one or more candidate first polypeptides with one or more candidate second polypeptides in the presence of one or more ligands,
- (b) selecting a complex of the three components;
- (c) optionally isolating and/or identifying the unknown components of the complex;

(d) comparing the binding of the first polypeptide component of the complex to the second polypeptide component of the complex in the presence and absence of the ligand component of the complex; and

(e) selecting complexes where said binding differs in the presence and absence of the ligand component,

in which at least one component is provided in the form of a library of members.

35. (withdrawn): A method of regulating transcription from a nucleic acid sequence comprising providing a target nucleic acid to which a nucleic acid binding protein selected by the method according to claim 33 binds and binding the nucleic acid binding protein to the target nucleic acid, thereby regulating transcription.

36 and 37. (canceled).

38. (currently amended): A method of modulating the expression of one or more genes, said method comprising administering a ~~nucleic acid binding protein and a ligand selected according to a method~~ switching system according to Claim ~~34~~ 33 to a cell, in which the regulatory sequences of the genes comprise a target nucleic acid to which the ~~nucleic acid binding protein~~ switching system binds in a manner modulatable by a ligand.

39. (currently amended): A method of modulating the expression of one or more nucleotide sequences of interest in a host cell which host cell comprises a first nucleic acid sequence capable of directing the expression of a ~~nucleic acid binding protein~~ the first polypeptide of the switching system according to Claim 34, a second nucleic acid sequence capable of directing the expression of a the second polypeptide of the switching system of according to Claim 34, ~~the binding between the nucleic acid binding to the second polypeptide being modulatable by a ligand~~, and a target nucleic acid sequence to which the at least one of the first or second polypeptides of the switching system binds ~~nucleic acid binding protein binds in a manner modulatable by a second polypeptide~~, which method comprises administering said ligand to the cell.

40. (withdrawn): A method according to Claim 39, in which the at least one DNA-binding polypeptide component of the switching system ~~nucleic acid binding protein~~ is heterologous to the host cell.

41. (withdrawn): A method according to Claim 39 wherein the host cell is a plant cell.

42. (withdrawn): A method according to Claim 41, in which the plant cell is part of a plant and the target sequence is part of a regulatory sequence to which the nucleotide sequence of interest is operably linked, said regulatory sequence being preferentially active in the male or female organs of the plant.

43. (withdrawn): A non human transgenic organism comprising a target nucleic acid sequence, a first nucleic acid sequence capable of directing the expression of a nucleic acid binding protein, and a second nucleic acid sequence capable of directing the expression of a second polypeptide which binds to the nucleic acid binding protein in a manner modulatable by a ligand, in which the nucleic acid binding protein binds to the target nucleic acid sequence in a manner modulatable by binding of the second polypeptide.

44. (withdrawn): An organism according to Claim 43, in which any or all of the first nucleic acid sequence, the second nucleic acid sequence, and the target nucleic acid sequence are heterologous to the organism.

45. (withdrawn): A transgenic nonhuman organism according to Claim 43 which is a plant.

46. (currently amended): A method according to claim 1, in which the first ~~molecule~~ polypeptide component of the complex has a higher affinity for the second ~~molecule~~ polypeptide component of the complex in the presence of the ligand component than in the absence of the ligand component.

47. (currently amended): A method according to claim 1, in which the first ~~molecule~~ polypeptide component of the complex has a higher affinity for the second ~~molecule~~ polypeptide component of the complex in the absence of the ligand component than in the presence of the ligand component.